CLAIMS

WHAT IS CLAIMED IS:

1. A method for determining a preferred alignment between a query sequence and at least one template sequence comprising the steps of:

5   a.   aligning at least two reference sequences to determine one or more BRIDGE/BULGE gaps;

      b.   determining at least one alignment score between the potential alignment of said query sequence and each said template sequence; wherein each said alignment score reflects whether said alignment between said query sequence and

10   each said template sequence creates a BRIDGE/BULGE gap; and

      c.   determining a preferred alignment between said query sequence and each said template sequence based on said alignment score.

2. The method of claim 1 wherein said preferred alignment is the optimal alignment.

3. The method of claim 1. wherein step b comprises the steps of:

15   a.   forming a sequence alignment similarity matrix for said query sequence and each said template sequence with matrix elements s_{ij}; and

      b.   determining a sequence alignment sum matrix with matrix elements S_{ij} from the dynamic evolution of each said sequence alignment similarity matrix, wherein the matrix elements of each said sum matrix reflect whether or not any

20   potential alignment gaps that may be formed from the alignment of said query sequence with each said template sequence creates a BRIDGE/BULGE gap.

4. The method of claim 3. wherein step b comprises the steps of:

a.   calculating said sequence alignment sum matrix from the dynamic

evolution of each said sequence alignment similarity matrix, according to the

equation:

5      $S_{ij} = s_{ij} + Max\{S_{i+1,j+1}, S_{i+1,j+2\ to\ jmax} - GAP, S_{i+2\ to\ imax,j+2} - GAP, S_{m,n} -$

BRIDGE/BULGE$\}$,

wherein GAP represents the gap penalty for an alignment gap between said query

sequence and each said template sequence, BRIDGE/BULGE represents the

10   penalty for a known bridge or bulge that begins at the m,n matrix element of said

sum matrix and ends at the i,j matrix element of said sum matrix and $Max\{S_{i+1,j+1},$

$S_{i+1,j+2\ to\ jmax} - GAP, S_{i+2\ to\ imax,j+2} - GAP, S_{m,n} - BRIDGE/BULGE\}$ refers to the

maximum value of the four terms contained within the brackets

5.   A method for determining a preferred alignment between a query sequence and at

15   least one template sequence comprising the steps of:

a.   aligning at least two reference sequences to determine at least one

BRIDGE/BULGE gap;

b.   forming a sequence alignment similarity matrix from said query sequence

and each said template sequence;

20   c.   determining a sequence alignment sum matrix from the dynamic evolution

of each said sequence alignment similarity matrix, wherein the matrix elements of

each said sum matrix reflect whether or not any potential alignment gaps that may

be formed from the alignment of said query sequence with each said template

sequence creates a BRIDGE/BULGE gap; and

d.   determining a preferred alignment between said query sequence and each

said template sequence from said dynamic evolution of each said sum matrix.

5   6.   The method of claim 5 wherein said preferred alignment is the optimal alignment.

7.   A method for determining a preferred alignment between a query sequence and at

least one template sequence comprising the steps of:

a.   aligning at least two reference sequences to determine at least one

BRIDGE/BULGE gap;

10   b.   calculating a sequence alignment similarity matrix with matrix elements s_{ij}

for said query sequence and each said template sequence;

c.   calculating a sequence alignment sum matrix with matrix elements S_{ij}

from the dynamic evolution of each said sequence alignment similarity matrix,

according to the equation:

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$$S_{ij} = s_{ij} + \text{Max}\{S_{i+1,j+1}, S_{i+1,\,j+2\,\text{to jmax}} - GAP, S_{i+2\,\text{to imax},\,j+2} - GAP, S_{m,n} -$$

BRIDGE/BULGE$\}$,

wherein GAP represents the gap penalty for an alignment gap between said query

20   sequence and each said template sequence, BRIDGE/BULGE represents the

penalty for a known bridge or bulge that begins at the m,n matrix element of said

sum matrix and ends at the i,j matrix element of said sum matrix and Max$\{S_{i+1,j+1},$

$S_{i+1, j+2 \text{ to } jmax} - GAP$, $S_{i+2 \text{ to } imax, j+2} - GAP$, $S_{m,n} - BRIDGE/BULGE\}$ refers to the maximum value of the four terms contained within the brackets; and

d.   determining a preferred alignment between said query sequence and each said template sequence from the dynamic evolution of said sum matrix.

5   8.   The method of claim 7 wherein said preferred alignment is an optimal alignment.

9.   A method for determining a preferred alignment between at least one query sequence and at least one template sequence, for use in primary sequence homology modeling methods, comprising the steps of:

a.   aligning at least two reference sequences to determine one or more

10   BRIDGE/BULGE gaps;

b.   determining at least one alignment score for the potential alignment of each said query sequence and each said template sequence; wherein each said alignment score reflects whether said alignment between each aid query sequence and each said template sequence creates a BRIDGE/BULGE gap; and

15   c.   determining a preferred alignment between each said query sequence and each said template sequence based on said alignment scores, wherein said preferred alignment contains from approximately 10% to approximately 20% homologous residues.

10.   The method of claim 9 wherein said preferred alignment is the optimal alignment.

20   11.   The method of claim 9 wherein said primary sequence homology method is a method for determining the three dimensional structure of said query sequence.

12.   The method of claim 10 wherein said primary sequence homology modeling

method is a method for determining the three dimensional structure of said query

sequence.

13.   The method of claim 9 wherein said primary sequence homology modeling

5   method is a method for determining the primary sequence homology relationship

between at least two query sequences.

14.   The method of claim 10 wherein said primary sequence homology modeling

method is a method for determining the sequence homology relationship between at least

two query sequences.

10   15.   A method for determining a preferred alignment between at least one query

sequence and at least one template sequence, for use in primary sequence homology

modeling methods, comprising the steps of:

      a.   aligning at least two reference sequences to determine at least one

      BRIDGE/BULGE gap;

15   b.   forming a sequence alignment similarity matrix for each said query

      sequence and each said template sequence;

      c.   determining a sequence alignment sum matrix from the dynamic evolution

      of each said sequence alignment similarity matrix, wherein the matrix elements of

      each said sum matrix reflect whether or not any potential alignment gaps that may

20   be formed from the alignment of each said query sequence with each said

      template sequence creates a BRIDGE/BULGE gap; and

      d.   determining a preferred alignment between each said query sequence and

      each said template sequence from said dynamic evolution of each said sum

matrix, wherein said preferred alignment contains from approximately 10% to approximately 20% homologous residues.

16. The method of claim 15 wherein said preferred alignment is the optimal alignment.

5 17. The method of claim 15 wherein said primary sequence homology method is a method for determining the three dimensional structure of said query sequence.

18. The method of claim 16 wherein said primary sequence homology modeling method is a method for determining the three dimensional structure of said query sequence.

10 19. The method of claim 15 wherein said primary sequence homology modeling method is a method for determining the primary sequence homology relationship between at least two query sequences.

20. The method of claim 16 wherein said primary sequence homology modeling method is a method for determining the primary sequence homology relationship

15 between at least two query sequences.

21. A method for determining a preferred alignment between at least one query sequence and at least one template sequence, for use in primary sequence homology modeling methods, comprising the steps of:

a. aligning at least two reference sequences to determine at least one

20 BRIDGE/BULGE gap;

b. calculating a sequence alignment similarity matrix with matrix elements s_{ij} for each said query sequence and each said template sequence;

c.   calculating a sequence alignment sum matrix with matrix elements S_{ij} from the dynamic evolution of each said sequence alignment similarity matrix, according to the equation:

5    $S_{ij} = s_{ij} + Max\{S_{i+1,j+1}, S_{i+1, j+2\,to\,jmax} - GAP, S_{i+2\,to\,imax, j+2} - GAP, S_{m,n} - BRIDGE/BULGE\}$,

wherein GAP represents the gap penalty for an alignment gap between said query sequence and each said template sequence, BRIDGE/BULGE represents the

10   penalty for a known bridge or bulge that begins at the m,n matrix element of said sum matrix and ends at the i,j matrix element of said sum matrix and $Max\{S_{i+1,j+1}, S_{i+1, j+2\,to\,jmax} - GAP, S_{i+2\,to\,imax, j+2} - GAP, S_{m,n} - BRIDGE/BULGE\}$ refers to the maximum value of the four terms contained within the brackets; and

d.   determining a preferred alignment between each said query sequence and each

15   said template sequence from the dynamic evolution of said sum matrix; wherein said preferred alignment contains from approximately 10% to approximately 20% homologous residues.

22.   The method of claim 21 wherein said preferred alignment is the optimal alignment.

20   23.   The method of claim 21 wherein said primary sequence homology modeling method is a method for determining the three dimensional structure of said query sequence.

24.   The method of claim 22 wherein said primary sequence homology modeling method is a method for determining the three dimensional structure of said query sequence.

25.   The method of claim 21 wherein said primary sequence homology modeling

5   method is a method for determining the primary sequence homology relationship between at least two query sequences.

26.   The method of claim 22 wherein said primary sequence homology modeling method is a method for determining the primary sequence homology relationship between at least two query sequences.

10   27   A method for determining the three dimensional structure of a query sequence based upon primary sequence homology modeling with at least one template sequence, wherein, said alignment between said query sequence and said template sequence is determined by the methods of claim 2, claim 6, claim 8, claim 12, claim 20 and claim 24.

28.   A method for determining the primary sequence homology relationship between

15   at least two query sequences based upon primary sequence homology modeling with at least one template sequence, wherein, said alignment between said query sequence and said template sequence is determined by the methods of claim 2, claim 6, claim 8, claim 14, claim 22, and claim 26.